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| 09/869,612 | 11/13/2001 | Alesandro Massimo Gianni | GIANNI=1 | 5788 |

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EXAMINER

HAMUD, FOZIA M

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1647

9

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary

Application No.

09/869,612

Applicant(s)

GIANNI, ALESSANDRO MASSIMO

Examiner

Fozia M Hamud

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 1,3,14-16,27-30 and 32-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,4-13,17-26,31 and 55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the invention of Group II (claims 2, 4-13, 17-26, 31 and 55) in Paper No.8 filed on 02 July 2003 is acknowledged. No species election is necessary since neither claim 16 nor claim 35, which recite multiple species is elected.

Applicant's first ground of traversal is that there is no lack of unity of invention and this Application complies with PCT rules 13.1 and 13.2, since the no lack of unity was held during the international preliminary examination. Thus, Applicant alleges that this restriction requirement is in violation of the Patent Cooperation Treaty to which the United States is a signatory. Applicant's second grounds of traversal is that, even under U.S. law, the PTO has no authority to take the position that a single claim calls for more than one invention, (claims 18-26, 55 are listed in all four groups, except in the sense that such claims are generic and subject matter falling there within being species.

Applicant's first ground of traversal is not found persuasive. Firstly, each Application is searched and examined on its own merits. Secondly, the inventions listed as Groups I-IV do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1, because they are distinct and dissimilar methods that use different products and are practiced with materially different process steps.

With respect to Applicant's second grounds of traversal, claims 18-26 and 55, (~~Similarly claims 4-13~~), are multiply dependant claims, which depend from claims that are drawn to distinct inventions, therefore, these claims belong in more than one group. The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1, 3, 14-16, 27-30, 32-54 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions. Claims 4-13, 18-19, 21-26 and 55 will be searched and examined so far as they relate to a method of preparation of a population of circulating cells by administering to a donor a composition comprising growth hormone and G-CSF.

Specification:

2. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (e) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.

- (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) BRIEF SUMMARY OF THE INVENTION.
 - (g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
 - (h) DETAILED DESCRIPTION OF THE INVENTION.
 - (i) CLAIM OR CLAIMS (commencing on a separate sheet).
 - (j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
 - (k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

A section entitled "legend of the figures" is placed on page 49 of the instant specification, however, this section should be entitled "Brief Description of the Figures" and should be placed between a section entitled "Brief Summary of the Invention" and a section entitled "Detailed Description of the Invention". Appropriate correction is required.

Claim rejections-35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 2, 4-13, 17-26, 31 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing CD34+ cells in vivo said method comprising administering to a donor a composition comprising growth hormone and a composition comprising G-CSF, and isolating CD34+ cells from said donor, is not enabling for a method of preparing populations of "all" possible circulating cells in vivo, by administering to a donor a composition comprising growth hormone derivatives or any factor inducing growth hormone release, and a

composition comprising G-CSF, and isolating said population of circulating cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, practice the invention commensurate in scope with these claims.

Instant claims 2 and 31 encompass a method of preparing populations of circulating cells capable of regenerating hematopoiesis in vivo, by administering G-CSF simultaneously or separately with "any one of growth hormone's derivatives or any factor inducing growth hormone release", however, instant specification discloses that the administration of G-CSF and recombinant human growth hormone (rhGH) to patients with relapsed Hodgkin's disease, resulted in doubling or tripling the mobilization of CD34+ cells in the blood stream and increasing the number of CD34+ leukapheresed cells, (see pages 55-58 and figure 2). Thus, instant specification only discloses the administration of G-CSF and rhGH, but does not disclose "a derivative" or "a factor that induces growth hormone release".

The criteria set forth in *Ex parte Forman* (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, Applicant only discloses the administration of rhGH with G-CSF to stimulate the CD34+

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cells, but does not disclose a derivative or a factor that induces growth hormone release. With respect to "population of cells capable of regenerating hematopoiesis, instant specification only discloses that the mobilization of CD34+ cells are increased, but no other cell types. Therefore, the quantity of experimentation to determine which growth hormone derivatives or factors that induce growth hormone release, to administer and which types of cells that are capable of regenerating hematopoiesis, are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine all of the growth hormone derivatives or factors that induce growth hormone release, that would cause the mobilization of cells that regenerate hematopoiesis, as is encompassed by the scope of the claims. The disclosure that rhGH is administered in conjunction with G-CSF stimulates the mobilization of CD34+ cells, is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass "all" possible growth hormone derivatives and factors that induce growth hormone release.

With respect to claims which reciting "a population of circulating cells capable of regenerating hematopoiesis", the specification is non-enabling for a population of circulating cells that are not able to regenerate hematopoiesis and are only capable of regenerating hematopoiesis, only if further modified, since Applicants have not taught how to further modify these cells such that these cells can regenerate hematopoiesis. It has been held that an element is "capable of" performing a function is not a positive

limitation but only requires the ability to perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69 USPQ 138.

3b. Claims 2, 4-13, 17-26 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Instant claims are drawn to a method of preparing populations of circulating cells capable of regenerating hematopoiesis in vivo, by administering to a donor a composition comprising growth hormone derivatives or any factor inducing growth hormone release, and a composition comprising G-CSF, and isolating said population of circulating cells. However, the specification does not provide a written description for a growth hormone derivative or any factor inducing growth hormone release, to be used in the claimed method. The specification discloses that the administration of G-CSF and recombinant human growth hormone (rhGH) to patients with relapsed Hodgkin's disease, resulted in doubling or tripling the mobilization of CD34+ cells in the blood stream and increasing the number of CD34+ leukapheresed cells, (see pages 55-58 and figure 2). Therefore, instant specification only describes the structure of rhGH to be used in the claimed method, but fails to describe a derivative of said growth hormone or a factor that induces the release of growth hormone to be used in the claimed method. The skilled artisan would not be able to visualize the structure derivative of said growth hormone or a factor that induces the release. Applicant must

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convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed. Therefore, the structure of the derivative of a growth hormone or a factor that induces the release to be used in the claimed method has not been disclosed in order, to satisfy the written description provision of 35 U.S.C. 112, first paragraph. As a result, it does not appear that the inventors were in possession of a derivative of growth hormone or a factor that induces the release to be used in the claimed method.

Claim rejections-35 USC § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 4-13, 17-26, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 4-13 and 17-19, 21-26 and 55, depend on non-elected claims 1 or 3, which renders the claims indefinite. Appropriate correction is required.

Claim rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4a. Claims 2, 4-13, 17-26, 31 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable Haas et al (1995) in view of Murphy et al (1992).

Haas et al teach that the administration of G-CSF during steady state hematopoiesis or following cytotoxic chemotherapy leads to an increase of hematopoietic progenitor cells in peripheral blood, (see abstract). Haas et al showed that the administration of G-CSF increased the level of circulating CD34+ cells. Haas et al showed that the administration of G-CSF to donors caused a median increase of 6.5 to 100 fold increase of circulating CD34+ cells, (see page 2541, column 2). Haas et al also teach a method of characterizing and measuring the hematopoietic progenitor cells after G-CSF administration, (see page 250, bottom of column 2).

However, Haas et al do not teach that the administration of growth hormone simultaneously or separately with G-CSF stimulates circulating CD34+ cells.

Murphy et al disclose that the administration of recombinant human growth hormone (rhGH) leads to the stimulation of splenic and bone marrow hematopoietic progenitor cell content, (see abstract and page 1444, column 1).

Instant claim 2 is drawn to a method of preparing a population of circulating cells by administering growth hormone and G-CSF to a donor and isolating said cells, and claims 4-13, 17-26 and 55 limit the dosage of the growth hormone and G-CSF per body weight, the cell type and to be prepared and cell number.

Therefore, it would have been obvious at the time the instant case was filed, to combine the teachings of Haas et al and Murphy et al to define a method of preparing circulating progenitor cells by administering G-CSF and growth hormone, because Haas

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et al teach that the administration of G-CSF increases the level of circulating CD34+ cells and Murphy et al teach the rhGH leads to the stimulation of splenic and bone marrow hematopoietic progenitor cell content . Administration of G-CSF and growth hormone would have been expected to cause stimulation of the number of circulating progenitor cells with a reasonable expectation of success, because prior art teaches that each of these products exerts a significant effect on hematopoietic progenitor cell.

. With respect to claims 4-13, 7-26, 31 and 55, it would have been obvious to optimize the dosage and harvesting schedules.

One of ordinary skill in the art would have been motivated to administer G-CSF and growth hormone to prepare circulating progenitor cells, because the use of blood-derived hematopoietic stem cells offers new modes of therapy for patients undergoing chemotherapy or radiation therapy.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Fozia Hamud
Patent Examiner
Art Unit 1647
16 October 2003

FH

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PRIMARY EXAMINER